PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 : A61F 2/14 — A1

(11) International Publication Number: WO 95/03755

(43) International Publication Date: 9 February 1995 (09.02.95)

(21) International Application Number: PCT/US94/08462

(22) International Filing Date: 28 July 1994 (28.07.94)

(30) Priority Data:
08/101,438 2 August 1993 (02.08.93) US

(60) Parent Application or Grant
(63) Related by Continuation
US 08/101,438 (CIP)
Filed on 2 August 1993 (02.08.93)

(71) Applicant *(for all designated States except US)*: KERAVISION, INC. [US/US]; 48630 Milton Drive, Fremont, CA 94538-7353 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: SILVESTRINI, Thomas, A. [US/US]; 1701 Las Trampas Road, Alamo, CA 94507 (US).

(74) Agents: CAGAN, Felissa, H. et al.; Morrison & Foerster, 755 Page Mill Road, Palo Alto, CA 94304-1018 (US).

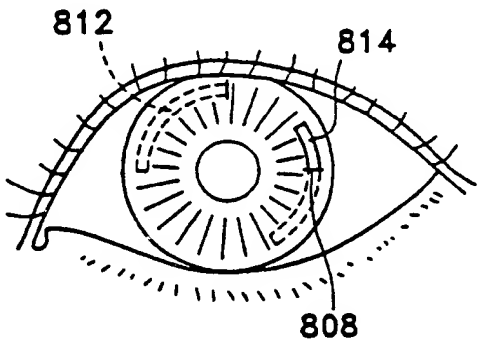
(81) Designated States: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: SEGMENTED PREFORMED INTRASTROMAL CORNEAL INSERT

(57) Abstract

This invention is a preformed intra-stromal corneal insert (812, 814). It is made of a physiologically compatible polymer and may be used to adjust corneal curvature and thereby correct vision abnormalities. The insert of segment (812, 814) may also be used to deliver therapeutic or diagnostic agents to the interior of the cornea, or of the eye. The insert (812, 814) subtends only a portion of a ring or "arc", encircling the anterior cornea outside of the cornea's field of view. The invention also includes a procedure for inserting the device into the cornea.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GB	United Kingdom	MR	Mauritania
AU	Australia	GE	Georgia	MW	Malawi
BB	Barbados	GN	Guinea	NE	Niger
BE	Belgium	GR	Greece	NL	Netherlands
BF	Burkina Faso	HU	Hungary	NO	Norway
BG	Bulgaria	IE	Ireland	NZ	New Zealand
BJ	Benin	IT	Italy	PL	Poland
BR	Brazil	JP	Japan	PT	Portugal
BY	Belarus	KE	Kenya	RO	Romania
CA	Canada	KG	Kyrgystan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic of Korea	SD	Sudan
CG	Congo			SE	Sweden
CH	Switzerland	KR	Republic of Korea	SI	Slovenia
CI	Côte d'Ivoire	KZ	Kazakhstan	SK	Slovakia
CM	Cameroon	LI	Liechtenstein	SN	Senegal
CN	China	LK	Sri Lanka	TD	Chad
CS	Czechoslovakia	LU	Luxembourg	TG	Togo
CZ	Czech Republic	LV	Latvia	TJ	Tajikistan
DE	Germany	MC	Monaco	TT	Trinidad and Tobago
DK	Denmark	MD	Republic of Moldova	UA	Ukraine
ES	Spain	MG	Madagascar	US	United States of America
FI	Finland	ML	Mali	UZ	Uzbekistan
FR	France	MN	Mongolia	VN	Viet Nam
GA	Gabon				

SEGMENTED PRE-FORMED INTRASTROMAL CORNEAL INSERT

Field of the Invention

This invention is a pre-formed intrastromal corneal insert. It is made of a physiologically compatible polymer and may be used to adjust corneal curvature and thereby correct vision abnormalities. The insert or segment may also be used to deliver therapeutic or diagnostic agents to the interior of the cornea or of the eye. The insert subtends only a portion of a ring, or "arc", encircling the anterior cornea outside of the cornea's field of view but within the frontal circumference of the cornea, but may be used in multiples to form complete arcs or to form constructs of varying thicknesses. The invention also includes both a minimally invasive procedure for inserting one or more of the devices into the cornea as well as the thus-corrected eye.

Background of the Invention

Anomalies in the overall shape of the eye can cause visual disorders. Hyperopia ("farsightedness") occurs when the front-to-back distance in the eyeball is too short. In such a case, parallel rays originating greater than 20 feet from the eye focus behind the retina. In contrast, when the front-to-back distance of eyeball is too long, myopia ("nearsightedness") occurs and the focus of parallel rays entering the eye occurs in front of the retina. Astigmatism is a condition which occurs when the parallel rays of light do not focus to a single point within the eye, but rather have a variable

focus due to the fact that the cornea refracts light in a different meridian at different distances. Some degree of astigmatism is normal, but where it is pronounced, the astigmatism must be corrected.

Hyperopia, myopia, and astigmatism are usually corrected by glasses or contact lenses. Surgical methods for the correction of such disorders are known. Such methods include radial keratotomy (see, e.g., U.S. Patents Nos. 4,815,463 and 4,688,570) and laser corneal ablation (see, e.g., U.S. Patent No. 4,941,093).

Another method for correcting those disorders is through the implantation of polymeric rings (intrastromal corneal rings or "ICR's") in the eye's corneal stroma to change the curvature of the cornea. Previous work involving the implantation of polymethylmethacrylate (PMMA) rings, allograft corneal tissue, and hydrogels is well documented. One of the ring devices involves a split ring design which is inserted into a channel previously dissected in the stromal layer of the cornea. A minimally invasive incision is used both for producing the channel and for inserting the implant. See, for instance, the use of PMMA intrastromal rings in U.S. Patents Nos. 4,452,235 to Reynolds; 4,671,276 to Reynolds; 4,766,895 to Reynolds; and 4,961,744 to Kilmer et al. These documents suggest only the use of ICR's which completely encircle the cornea.

The use of soft polymers as intrastromal inserts is not widely known. For instance, U.S. Patent No. 5,090,955 to Simon, suggests an ICR which is made by introducing a settable polymer or gel into a previously made intrastromal channel. This procedure does not allow the surgeon to specify the precise size of the resulting ring nor is it a process which allows precise control of the pathway of the flowing polymer within the eye since

the gel must simply conform to the shape of the intrastromal channel. However, it does show the concept of using arcuate channels containing a gel-based insert centered about the corneal to correct.

Temirov et al, "Refractive circular tunnel keroplasty in the correction of high myopia", Vestnik Oftalmologii 1991: 3-21-31, suggests the use of collagen thread as ICR material.

These publications do not suggest the introduction of pre-formed polymeric arcuate inserts into the cornea for the correction of various visual aberrations. Certainly the publications do not imply that the devices may be used to introduce therapeutic or diagnostic materials into the corneal intrastromal space.

Summary of the Invention

This invention is a pre-formed polymeric insert suitable for insertion between the lamella of the corneal stroma. The insert is an arc-shaped segment of a ring and may be used in isolation, in isolated multiples, in cooperative multiples, as segments in a larger assemblage encircling at least a portion of the cornea, or as assemblages to form constructs of varying thickness. The insert may be of one or more synthetic or natural polymers, hydrophilic or hydrophobic, or may be a hybrid device comprising layered materials or it may be hollow.

The insert may be adapted to be fillable with a biologic agent, drug or other liquid, emulsified, or time-release eye treatment or diagnostic material.

When the insert is a hybrid, both the inner and outer portions may comprise variously one or more high or low modulus, physiologically compatible polymers or a composite of a low modulus polymer and a high modulus polymer. The inner portion may comprise a gel or a

polymeric material which is polymerized *in situ* after introduction into a hollow center layer.

These inventive segmented inserts may be introduced into the corneal stroma using techniques involving the steps of providing an intrastromal channel which traverses at least a portion of the circumcorneal rotation. Specific indications, such as astigmatism, may be rectified by insertion of one or more of the inserts into a partial intrastromal channel to flatten the steeper portions of the anterior corneal surface without insertion of a complete intracorneal ring (ICR).

If hydratable polymers are used, they may be hydrated before or after introduction into the intrastromal passageway created by the surgical device used to introduce these devices into the eye. If the outer layer is hydrated before insertion into the eye, the final size of the insert is set before that insertion. If the hydratable polymers are allowed to hydrate within the corneal space, the device (if appropriate polymers are chosen) will swell within the eye to its final size. If prehydrated, the outer layer often provides a measure of lubricity to the device, allowing it to be inserted with greater ease. Other of the noted low modulus polymers may also provide such lubricity.

Brief Description of the Drawings

Figure 1 is a schematic illustration of a horizontal section of the eye.

Figure 2 is a schematic illustration of the anterior portion of the eye showing the various layers of the cornea.

Figures 3A and 3B show respectively a front view and a cross section of a typical intracorneal insert

made according to the invention which shows certain defined terms used in the description.

Each of Figures 4A, 4B, and 4C; 5A, 5B and 5C; 6A, 6B, and 6C; and 7A, 7B, and 7C, shows respectively a front view ("A"), a cross section ("B"), a top view ("C") of various narrow point intracorneal inserts made according to the invention.

Figures 8A, 8B, and 8C show respectively a front view and two cross sections of a broad point tapered intracorneal insert made according to the invention.

Figures 9A, 9B, and 9C show respectively a front view and two cross sections of a soft, filled intracorneal insert made according to the invention.

Figure 10 depicts a front view of an end-to-end assemblage of intracorneal segments having no end junctions between the inserts.

Figure 11 shows a front view of an end-to-end assemblage of intracorneal segments having junctions between the inserts to hold them in a particular spatial relationship.

Figure 12 shows a partial cross-sectional view of an end-to-end assemblage of intracorneal segments which are strung on a filament to form a ring.

Figures 13A and 13B show respectively a front view and a cross section of an assemblage of intracorneal inserts made according to the invention which overlap at their ends to form a single monolithic device.

Figures 14A-14E and 15A-15F schematically depict procedures for installing intracorneal inserts.

Description of the Invention

Prior to explaining the details of the inventive devices, a short explanation of the physiology of the eye is needed to appreciate the functional

relationship of these intracorneal inserts or segments to the eye.

Figure 1 shows a horizontal cross-section of the eye with the globe (11) of the eye resembling a sphere with an anterior bulged spherical portion representing the cornea (12).

The globe (11) of the eye consists of three concentric coverings enclosing the various transparent media through which the light must pass before reaching the light-sensitive retina (18). The outermost covering is a fibrous protective portion the posterior five-sixths of which is white and opaque and called the sclera (13), and sometimes referred to as the white of the eye where visible to the front. The anterior one-sixth of this outer layer is the transparent cornea (12).

A middle covering is mainly vascular and nutritive in function and is made up of the choroid, ciliary body (16), and iris (17). The choroid generally functions to maintain the retina (18). The ciliary body (16) is involved in suspending the lens (21) and accommodation of the lens. The iris (17) is the most anterior portion of the middle covering of the eye and is arranged in a frontal plane. It is a thin circular disc similar in function to the diaphragm of a camera, and is perforate near its center by a circular aperture called the pupil (19). The size of the pupil varies to regulate the amount of light which reaches the retina (18). It contracts also to accommodation, which serves to sharpen the focus by diminishing spherical aberration. The iris divides the space between the cornea (12) and the lens (21) into an anterior chamber (22) and posterior chamber (23). The innermost portion of covering is the retina (18), consisting of nerve elements which form the true receptive portion for visual impressions.

The retina (18) is a part of the brain arising as an outgrowth from the fore-brain, with the optic nerve (24) serving as a fiber tract connecting the retina part of the brain with the fore-brain. A layer of rods and cones, lying just beneath a pigmented epithelium on the anterior wall of the retina serve as visual cells or photoreceptors which transform physical energy (light) into nerve impulses.

The vitreous body (26) is a transparent gelatinous mass which fills the posterior four-fifths of the globe (11). At its sides it supports the ciliary body (16) and the retina (18). A frontal saucer-shaped depression (27) houses the lens.

The lens (21) of the eye is a transparent bi-convex body of crystalline appearance placed between the iris (17) and vitreous body (26). Its axial diameter varies markedly with accommodation. A ciliary zonule (273), consisting of transparent fibers passing between the ciliary body (16) and lens (21) serves to hold the lens (21) in position and enables the ciliary muscle to act on it.

Referring again to the cornea (12), this outermost fibrous transparent coating resembles a watch glass. Its curvature is somewhat greater than the rest of the globe and is ideally spherical in nature. However, often it is more curved in one meridian than another giving rise to astigmatism. A central third of the cornea is called the optical zone with a slight flattening taking place outwardly thereof as the cornea thickens towards its periphery. Most of the refraction of the eye takes place through the cornea.

Figure 2 is a more detailed drawing of the anterior portion of the globe showing the various layers of the cornea (12) making up the epithelium (31). Epithelial cells on the surface thereof function to

maintain transparency of the cornea (12). These epithelial cells are rich in glycogen, enzymes, and acetylcholine and their activity regulates the corneal corpuscles and controls the transport of water and electrolytes through the lamellae of the stroma (32) of the cornea (12).

An anterior limiting lamella (33), referred to as Bowman's membrane or layer, is positioned between the epithelium (31) and the stroma (32) of the cornea. The stroma (32) are made up of lamellae having bands of fibrils parallel to each other and crossing the whole of the cornea. While most of the fibrous bands are parallel to the surface, some are oblique, especially anteriorly. A posterior limiting lamella (34) is referred to as Descemet's membrane. It is a strong membrane sharply defined from the stroma (32) and resistant to pathological processes of the cornea.

The endothelium (36) is the most posterior layer of the cornea and consists of a single layer of cells. The limbus (37) is the transition zone between the conjunctiva (38) and sclera on the one hand and the cornea (12) on the other.

Figure 3A shows a front view of a typical insert made according to the invention and Figure 3B shows a cross section of that insert. These segments are suitable for insertion into the appropriately prepared interlamellar, intrastromal, intracorneal channel of the eye. Generally the intrastromal segment is installed in the following manner: A small radial incision is made at the corneal radius in which the intrastromal segment is ultimately to be installed about the cornea. A dissector in the form of a split ring having a point suitable for producing the interlamellar channel in the corneal stroma is introduced into the stromal space through the small incision. It is then rotated in such a fashion that a

generally semicircular or arc-shaped channel is formed partially circling the cornea at the chosen radius. The dissector is then rotated in the opposite direction to withdraw it from the tunnel or channel thus formed. An intrastromal segment is then introduced into the channel.

As is shown in Figure 3A, the arcuate segment (300) is a portion of the circle and subtends some specific amount of a circumference of the cornea (at some chosen radius) equal to a value of "α", which value is less than 360°, preferably less than 320°, most preferably less than 270°. I refer to this angle as the "arc angle". The value of "α" is dependent upon the indication to be resolved and the physical arrangement of the segment (or segments) as they are installed in the eye. For instance, often the value of "α" is 60 to 90° for the correction of modest astigmatic aberrations. In any event, for definitional purposes, the opposite ends of a single "segment" do not meet when the segment is inserted into an intrastromal channel.

Similarly, if the segments are joined or used in conjunction with each other (such as are described in discussing Figures 10, 11, and 12 below) the value of "α" may be any of a wide range of values up to and including 360° or more.

Similarly, Figure 3B shows an orientation angle "β" of the segment as it is placed in the eye. Generally, the angle "β" is the angle between the tangent of the backside (302) of the segment (300) and the mean midline (304) of the eye. if the segment were (300) to be a continuous ring encircling the cornea, it would be known as a cone angle. For convenience, the chosen conventions for thickness and width are shown on Figure 3B.

We have found that for the majority of uses to which these inserts are intended, the value of "β" may be

between 0° and 90°, preferably between 20° and 45°. Generally, the value of "β" will be about 11° to 38°.

Further, the typical width is often between 0.005 inches and 0.250 inches. The typical thickness is often between 0.005 inches and 0.080 inches. Both of these parameters (along with certain other variables such as the cross-sectional shape of the device and its constituent polymers) determine, in large part, the level of correction achievable by use of a selected insert.

The materials used in these inserts may be relatively stiff (high modulus of elasticity) physiologically acceptable polymers such as polymethylmethacrylate (PMMA), TEFLON, polycarbonate, polysulfones, epoxies, or polyolefins such as polyethylene, polypropylene, polybutylene, and their mixtures and interpolymers. By "high modulus of elasticity", I mean moduli greater than about 3.5 kpsi. Many of these polymers are known in the art to be appropriately used in hard contact lenses. Obviously, any polymer which is physiologically suitable for introduction into the body is useful in the inserts of this invention. Many of the listed polymers are known to be suitable as hard contact lenses. For instance, PMMA has a long history in ophthalmological usage and consequently is quite desirable for use in these inserts.

Additionally, the polymeric material making up the segment may be low modulus polymers, e.g., those having a modulus of elasticity below about 3.5 kpsi, more preferably between 1 psi and 1 kpsi, and most preferably between 1 psi and 500 psi, which are physiologically compatible with the eye. Most polymeric materials used in soft contact lenses are suitable the segments of this invention. The class includes physiologically compatible elastomers and such crosslinked polymeric gels as polyhydroxyethylmethacrylate (Poly-HEMA) or

polyvinylpyrrolidone (PVP), polyethylene oxide, or polyacrylates, polyacrylic acid and its derivatives, their copolymers and interpolymers, and the like as well as biologic polymers such as crosslinked dextran, crosslinked heparin, or hyaluronic acid.

In many instances, the intrastromal segments may be hybrid, that is to say, the segments are made up of a number of polymeric layers typically with a soft or hydratable polymer on their outer surface. These hybrid segments will be described with greater particularity below. Partially hydrated or fully hydrated hydrophilic polymers are typically slippery and consequently may contribute to the ease with which the insert may be introduced into the interlamellar tunnel. It is usually desirable to (at least partially) hydrate the hybrid intrastromal segment in that, otherwise, the intrastromal segment during its traverse through the tunnel may desiccate the path and begin to stick to the interior wall of the tunnel. Suitable hydrophilic polymers include polyhydroxyethylmethacrylate (pHEMA), N-substituted acrylamides, polyvinylpyrrolidone (PVP), polyacrylamide, polyglycerylmethacrylate, polyethyleneoxide, polyvinyl alcohol, polyacrylic acid, polymethacrylic acid, poly (N, N-dimethyl amino propyl-N^1-acrylamide) and their copolymers and their combinations with hydrophilic and hydrophobic comonomers, crosslinks, and other modifiers. Thermoplastic hydrogels include hydropolyacrylonitrile, polyvinyl alcohol derivatives, hydrophilic polyurethanes, styrene-PVP block copolymers and the like.

The intrastromal segment may be lubricated with suitable ocular lubricants such as hyaluronic acid, methylethyl cellulose, dextran solutions, glycerine solutions, polysaccharides, or oligosaccharides upon its

introduction to help with the insertion particularly if one wishes to insert intrastromal segments of hydrophilic polymers without prior hydration. If a hybrid segment having a hydrophilic polymeric covering or a segment comprising a hydrophilic polymer is inserted into the eye without prior hydration, subsequent to the insertion, the intrastromal segment will swell to its final size or thickness within the eye. This swelling often permits the inclusion of larger intrastromal segments than would normally be accommodated within normal sized intrastromal channels.

Low modulus polymers used in this invention are often absorbent, particularly if they are hydratable, and may be infused with a drug or biologic agent which may be slowly released from the device after implantation of the intrastromal segment. For instance, the low modulus polymer may be loaded with a drug such as dexamethasone to reduce acute inflammatory response to implanting the device. This drug helps to prevent undesirable scarring or vascular ingrowth toward the intrastromal segment . Similarly, heparin, corticosteroids, antimitotics, antifibrotics, antiinflammatories, anti-scar-forming, anti-adhesion, and antiangiogenesis factors (such as nicotine adenine dinucleotide (NAD^+)) may be included to reduce or prevent angiogenesis and inflammation.

Clearly, there are a variety of other drugs suitable for inclusion in the intrastromal segment. The choice will depend upon the use to which the drugs are put.

Each of Figures 4A and 4B and 4C, 5A and 5B and 5C, 6A and 6B and 6C, and 7A and 7B and 7C, shows respectively a front view ("A" drawing) and a cross section ("B" drawing) and a side view ("C" drawing) of various narrow point intracorneal inserts made according

to the invention. Although these drawings show narrow points on the inventive inserts, such points are not a critical aspect of the invention. The ends of the inserts may be tapered in both width and thickness, in one or the other of those axes, or may be blunt. Other variations of the ends will be discussed below to the extent necessary to understand the invention. These inserts are "pre-formed" or "pre-shaped". By the use of these terms, I mean that the insert has sufficient structural integrity to approximate in shape some portion of the intrastromal channel into which it is to be placed.

Figure 4A shows a front view of a pre-shaped intracorneal insert (400) having ends (402). The intracorneal insert tapers both in width and in thickness to narrow points (402). Viewed in cross section in Figure 4B, the generally smooth convex front surface (404) and planar rear surface (406) may be seen. Figure 4C shows a side view of the segment or insert. Some care must be taken in using an insert having such narrowly pointed ends since such inserts are intended to be introduced into a previously created intrastromal channel. Points of great sharpness may wander in direction from the desired channel.

Figure 5A shows a front view of an intracorneal insert (500) having ends (502). Again, the intracorneal insert tapers both in width and in thickness to narrow points (502). Viewed in cross section in Figure 4B, the generally hexagonal shape may be seen. The surfaces most adjacent the anterior surface of the eye and the side just opposite are generally the two longer of the sides. Those generally planar front surface (504) and planar rear surface (506) may be seen. Our previous experience with Intracorneal Rings ("ICRs") has demonstrated that the use of such a shape in the cornea is generally less

traumatic than one of a rectangular cross section and yet, because of the similarity of the shape to that of the intrastromal formed by the blade producing the channel, is often considered to be the maximum cross sectional volume achievable in such configuration. Figure 5C shows a side view of the segment or insert.

Figure 6A shows a front view of an intracorneal insert (600) having ends (602). The intracorneal insert tapers both in width and in thickness to narrow points (502). Figure 6B shows the generally round cross section. The cross section may also be oval-shaped with the major axis of the oval either as the width or the thickness or neither. Figure 6C shows a side view of the segment or insert which, because of the symmetry of the device, is the same as the top view.

Figure 7A shows a front view of a hybrid intracorneal insert (700) having ends (702). Again, the intracorneal insert tapers both in width and in thickness to narrow points (702). Viewed in cross section in Figure 5B, the generally hexagonal shape may be seen. This set of Figures is to show the concept of a multilayered insert made up of polymers of different characteristics. In this example of a multi-layered insert, the hybrid intrastromal segment has inner (702) and outer faces (704) of polymers having low moduli of elasticity. Low modulus polymers are those having a modulus of elasticity below about 3.5 kpsi, more preferably between 1 psi and 1 kpsi, and most preferably between 1 psi and 500 psi. They must be physiologically compatible with the eye. As was noted above, this class of polymers includes most polymeric materials used in soft contact lenses.

The inner portion or core (706) as shown in Figure 7B may be a physiologically compatible polymer having a high modulus of elasticity. A high modulus of

elasticity is considered to be greater in value than about 3.5 kpsi, preferably 5-12 kpsi, and most preferably 8-10 kpsi. These high modulus of elasticity polymers are discussed above.

If hydratable polymers are chosen for the outside layers, the extent to which those outer layers swell upon hydration is dependent upon the type of polymer chosen and, when the polymer is hydratable, upon the amount of cross-linking found in the outer layers (702) and (706), and upon the thickness of the layer. Generally speaking, the more highly linked the hydratable polymer, the smaller the amount of volume change upon hydration. Conversely, a polymer having only sufficient cross-linking for strength in the service in which this device is placed, will have a somewhat lower level of cross-linking. Alternatively, a substantially nonswellable polymer system may be formed of a hydrogel physically interpenetrated by another polymer which does not hydrate, e.g., polyHEMA.

The thickness of the outer layer depends in large function upon the intended use of the intrastromal segment. If the outer layer is used to provide a swellable outer layer which does not add significantly to the size of the intrastromal segment or is used functionally as a lubricant layer, the other layer may be quite thin -- even to the point of a layer of minimum coverage, perhaps as thin as a single molecular layer.

Of course, the inner and outer layers need not be, respectively, low modulus and high modulus polymers but may instead be multiple layers of low modulus polymers including an outer hydrophilic polymer layer and an inner hydrophobic polymer; a variety of hydrophilic polymers; etc.

Additionally, the inventive device shown in Figures 7A to 7C need not have a inner (704) and outer

(702) layers over the entire intrastromal segment. For instance, to alleviate astigmatism, an intrastromal segment having a thicker portion and a substantially thinner portion may be desired. An intrastromal segment having an inner core of a high modulus polymer and an outer covering of a swellable polymer might be chosen. The surgeon would remove a portion of the intrastromal segment 's exterior coating or face prior to introducing the intrastromal segment into the eye. Further, and as will be discussed below in greater detail, hydrophilic polymers are more easily infused with therapeutic and diagnostic materials than are the high modulus materials. In the variation just noted, the insert may then be used to deliver the infused therapeutic and diagnostic materials in a greatly delimited of treatment or diagnostic area.

Figure 8A shows a front view of an wide end intracorneal insert (800) having ends (802). In this variation, the insert tapers only in thickness to form a spade-shaped end (802). Viewed in cross section in Figure 8B, the generic shape may be seen. Figure 8C shows the same shape but nearer to the end of the device. This set of Figures is to show the concept of a single-tapered end.

Figure 9A is a front quarter view of a variation of the intrastromal segment (900) made of a low modulus polymer system hydratable outer coating (902). Figure 9C shows the inner cavity (904). This intrastromal segment may be inserted into the intrastromal space created by the dissector as a covering on a tool similar to the dissector which created the intracorneal channel. Once in position the insertion tool is rotated out of the intrastromal segment leaving the shell within the stroma.

Figure 9C shows the inner cavity (904) which may be filled with a biologic, a drug or other liquid, or biologically active eye treatment material. These devices may be tied or pinched or crimped or otherwise connected at their point of insertion by known techniques.

The shell (902) may be injected with a settable soft polymer core, allowed to expand to a desired thickness, and set. Polymeric gels which do not polymerize in situ are preferred. Suitable injectable polymers are well known but include polyHEMA hydrogel, cross-linked collagen, cross-linked hyaluronic acid, siloxane gels, and organic-siloxane gels such as cross-linked methyl vinyl siloxane gels.

Figure 10 shows a variation of the invention in which an assemblage of the inventive intrastromal segments (950) are formed into a polymeric ring or, at least, into an assemblage which totals no more than 360° of corneal circumference when assembled into the intracorneal space. The two segments (950) depicted in Figure 10 may be of any of the individual variations shown in the Figures above and need not be connected in any way. The segments may be of similar or quite different configurations depending upon the indication to be remedied. Additionally, they may be inserted in separately produced intrastromal channels which may, or may not, be in communication within the cornea. Such individual insertion will be discussed in more detail below.

Figure 11 shows a similar assemblage in which the intracorneal segments (952) are held together using open holes (954) and a clip (956) which may be a simple wire or other suitable joining device. An assemblage such as is seen in Figure 11 may be advantageously

inserted from a single central opening, as will be described below.

Figure 12 shows a variation, an assemblage of segments, in which the sections (960) are strung together on a filament (962). The segments (960) have an open pathway along their length (see cutaway) which permits such stringing.

Figures 13A and 13B show a variation of the inventive intracorneal inserts in which two or more inserts overlap to form an assemblage. The top view shown in Figure 13A depicts the assemblage as found in the eye. The assemblage need not be formed of segments of the same or similar width or thickness or material of construction nor need the assemblage be limited to the semicircle shown in Figure 13A. Although a front-to-back assemblage of is depicted in Figure 13B, the junction between the sections (964 & 966) may be of any other design which is allows contact between the adjoining sections and remains relatively immobile after the placement in the cornea. For instance, the design shown in Figures 13A and 13B involves the use of a smooth interface. The intrastromal channel normally exerts substantial force against the assemblage and will maintain the segments in the depicted relational position within the eye. In addition, rather than overlapping, the inserts may be stacked one on top of the other to form a further assemblage.

Figures 14A-14E schematically portray a method for the insertion of the segments described above in which partial arc segments are introduced into separate sections of the corneal circumference outside of the "sight" area of that cornea.

In Figure 14A, the frontal view shows the iris (800) and the pupil (802). As was described above, the cornea is clear and is not visible in these drawings.

Insertion of the inventive device is a reasonably simple surgical procedure. An entry slit (804) is made radially into the cornea. A dissector blade is introduced into the entry slit (804) and turned in the direction of the arrow (806) to form a partial intrastromal channel of a desired length. A second entry slit (808) may then be made in the cornea and a second intrastromal channel be made in the direction of the arrow (810).

Figure 14C shows the introduction of the first inventive segment (812) into the first entry slit (808). Figure 14C shows the first segment (812) in its final resting position and the introduction of the second segment (814) into the second entry slit (808). Finally Figure 14E shows both first segment (812) and second segment (814) in their final position within the cornea. This demonstrates the flexibility of the procedure in that either left or right "hand" insertion is appropriate and the intrastromal channel need ont be a complete circle about the cornea. Further, it should be noted that the first segment (812) and the second segment (814) may be of differing diameters or of differing arc lengths depending upon the indication to be resolved.

Figures 15A-15F schematically portray a method for the insertion of the segments described above in which partial arc segments are introduced into separate sections of the corneal circumference outside of the "sight" area of that cornea through a single entry slit.

Figure 15A shows the making of the initial entry slit (840) radially into the cornea. A dissector blade is introduced into the entry slit (840) and turned in the direction of the arrow (842) to form a partial intrastromal channel of a desired length. As is shown in Figure 15B, a second intrastromal channel is made in the direction of the arrow (844) from the same entry slit (842).

Figure 15C shows the introduction of the first segment (846) into the entry slit (842). Figure 15D shows the first segment (846) in its final resting position. Figure 15D shows the introduction of the second segment (848) into the entry slit (840). Finally Figure 15F shows both first segment (846) and second segment (848) in their final position within the cornea.

Because of the nature of certain of these inserts, a large measure of adaptability is available in the process of inserting the devices. For instance, I have found that when using various inserts (particularly with ocular lubricants) that the inserts may be "pushed" nearly 180° around a previously created intrastromal channel for insertion and then easily removed, if so desired. This observation means that the following procedure may be used. The eye of a person having myopia and/or astigmatism may be measured to determine the proper amount of correction needed. From this information, the size and placement of one or more segments may then be chosen. For instance, the selected sections might be two inserts of 30° arc angle and 100 mils x 100 mils cross section at two opposing meridian. after insertion in the appropriate channels, the vision of the eye might again be measured. If insufficient correction of an indication is found, the insert may be withdrawn and a larger size selected and inserted. If an astigmatic aberration is introduced, the insert may be withdrawn (partially or completely) and trimmed prior to complete re-insertion. Such adjustability is not normally available when dealing with gel-based rings or with surgical techniques based on radial keratotomy.

The inserts may be useful in the treatment of astigmatism, myopia, or the combination of the two. In each case, segments of differing arc length are preferred. For the treatment of astigmatism where no

myopic correction is needed, segments of between about 20° and 90°, preferably between about 20° and 60° may be used. Where treatment of astigmatism and myopia is required, segments of between about 45° and 160°, preferably between about 60° and 90° may be used. For the treatment of myopia where no astigmatic enhancement is required, segments of between about 90° and 360°, preferably between about 90° and 270° may be used.

The terms and expressions which have been used in the description above are used only as terms of description and not of limitation. There is no intention of excluding equivalents of the features shown or described. It is recognized that one having ordinary skill in this art would perceive equivalence to the inventions claimed below, which equivalence would be within the spirit of the invention as expressed above.

I CLAIM AS MY INVENTION:

1. An insert suitable for introduction into the corneal stroma comprising a pre-shaped, physiologically compatible, polymeric segment adapted for introduction into an intrastromal intracorneal channel and having an arc angle less than 360° when inserted into the intrastromal channel.

2. The insert of claim 1 where the segment comprises an arc angle of less than about 320°.

3. The insert of claim 2 where the segment comprises an arc angle of less than about 270°.

4. The insert of claim 3 where the segment comprises an arc angle of 20 to 90°.

5. The insert of claim 2 where the segment comprises a low modulus physiologically compatible polymer.

6. The insert of claim 5 where the low modulus physiologically compatible polymer is selected from polyhydroxyethylmethacrylate (Poly-HEMA), polyvinylpyrrolidone (PVP), polyethylene oxide, or polyacrylates, polyacrylic acid and its derivatives, their copolymers and interpolymers, silicones, crosslinked dextran, crosslinked heparin, or hyaluronic acid.

7. The insert of claim 5 where the low modulus physiologically compatible polymer is selected from hydratable polymers which swell upon hydration,

hydratable polymer systems which do not swell upon hydration, and elastomers.

8. The insert of claim 2 where the segment comprises comprises a polymer having a high modulus of elasticity.

9. The insert of claim 8 in which the polymer having a high modulus of elasticity comprises a polymer selected from PMMA, TEFLON, polysulfones, polycarbonate, epoxies, a polyolefin selected from polyethylene, polypropylene, polybutylene, mixtures, or interpolymers.

10. The insert of claim 1 having a hollow inner fillable portion.

11. The insert of claim 10 where the hollow inner portion is fillable with a liquid.

12. The insert of claim 10 where the hollow inner portion is at least partially filled with a gel or a settable polymer, a drug or a biologic agent.

13. The insert of claim 12 where the gel or settable polymer is selected from polyHEMA hydrogel, cross-linked collagen, cross-linked hyaluronic acid, siloxane gels, polyvinyl pyrrolidone, and organic-siloxane gels.

14. The insert of claim 5 additionally comprising a drug or biologic agent.

15. The insert of claims 12 or 14 where the drug is selected from dexamethasone, heparin, corticosteroids, antimitotics, antifibrotics,

antiinflammatory, anti-scar-forming, anti-adhesion, antithrombogenic, and antiangiogenesis factors.

16. The insert of claim 1 additionally comprising an ocular lubricant.

17. The insert of claim 16 where the ocular lubricant is selected from hyaluronic acid, methylethylcellulose, dextran solutions, glycerine solutions, polysaccharides, or oligosaccharides.

18. The insert of claim 1 having a hollow inner axis.

19. The insert of claim 18 where the hollow inner axis is threadable with a filament.

20. The insert of claim 1 having ends which are joinable to another insert.

21. The insert of claim 20 where the ends may be overlapped or abutted to form an assemblage.

22. The insert of claim 21 where the ends may be overlapped to form an assemblage having a constant or varying thickness.

23. The insert of claim 1 comprising at least two polymeric layers.

24. The insert of claim 23 where at least one polymeric layer comprises a low modulus physiologically compatible polymer.

25. The insert of claim 23 where at least one polymeric layer comprises a high modulus physiologically compatible polymer.

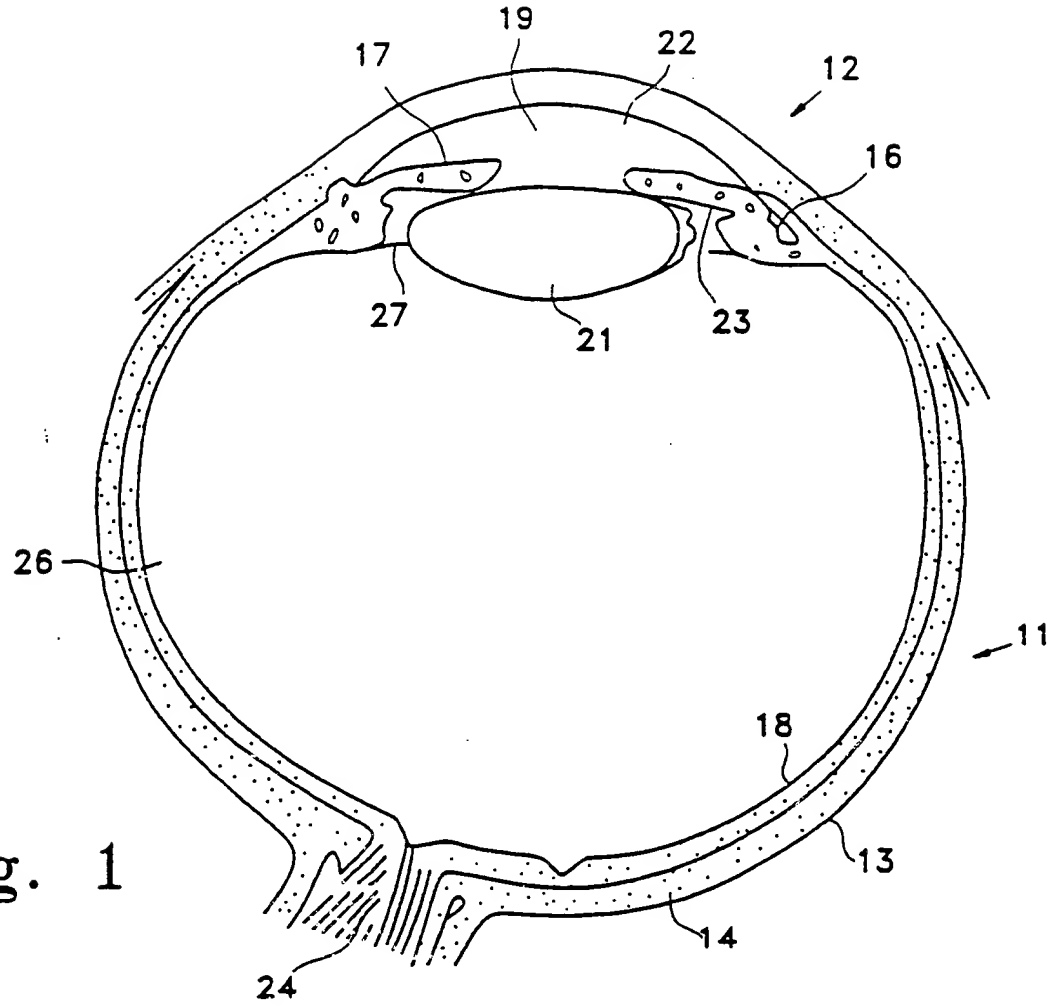


Fig. 1

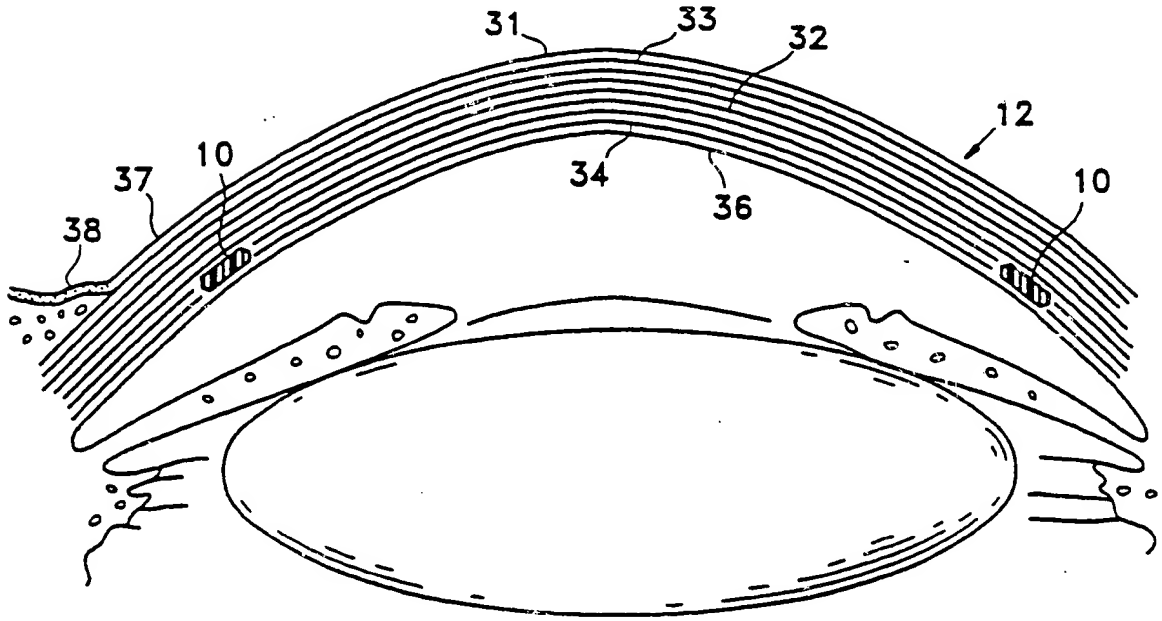


Fig. 2

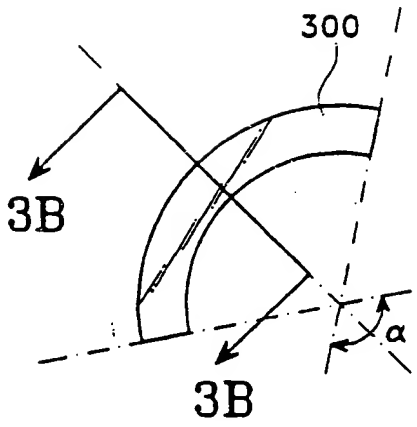


Fig. 3A

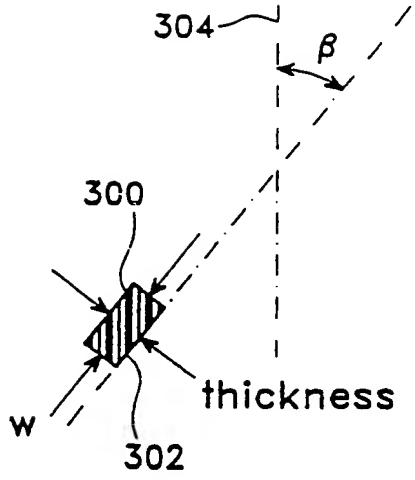


Fig. 3B

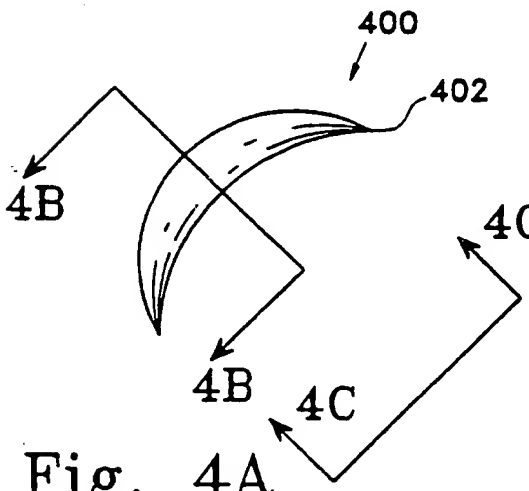


Fig. 4A

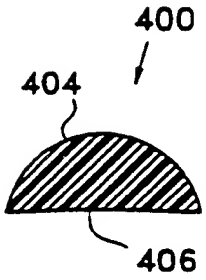


Fig. 4B

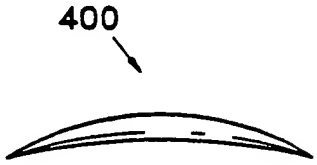


Fig. 4C

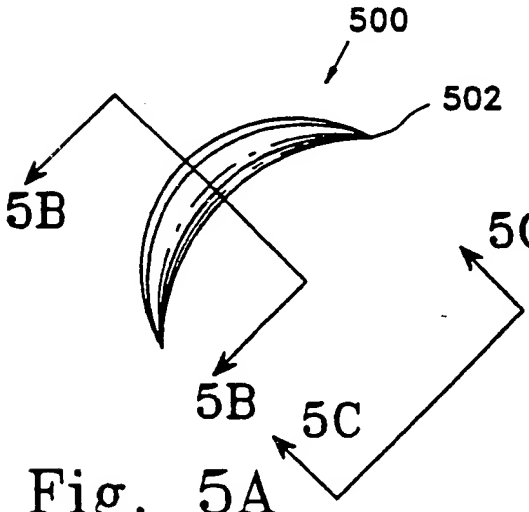


Fig. 5A

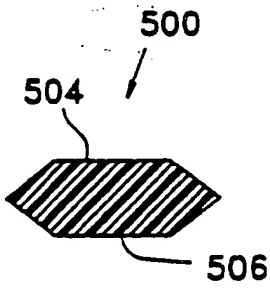


Fig. 5B

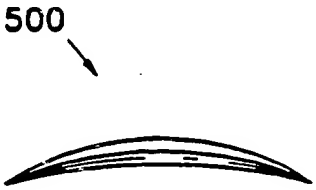


Fig. 5C

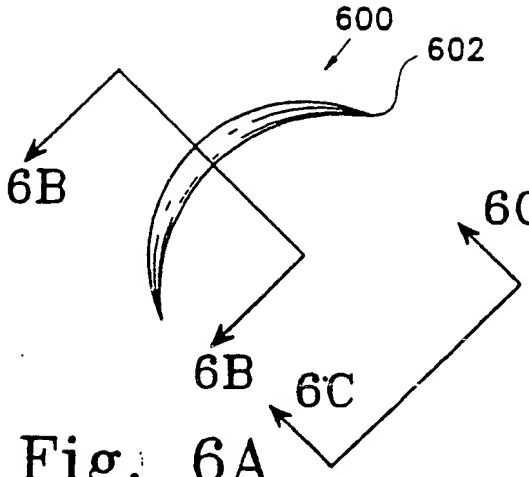


Fig. 6A

Fig. 6B

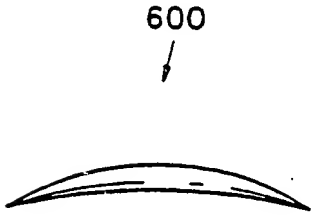


Fig. 6C

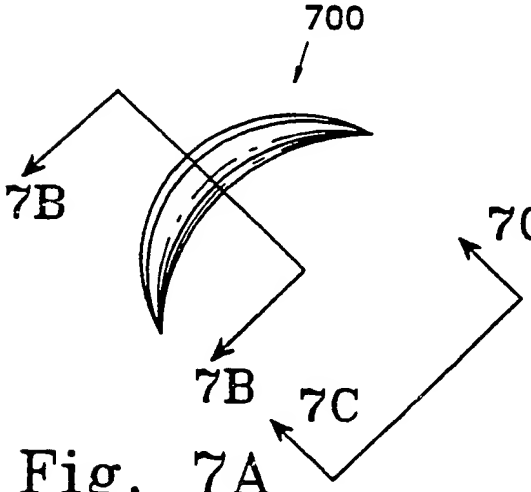


Fig. 7A

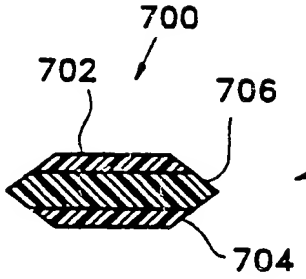


Fig. 7B

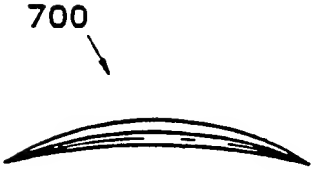


Fig. 7C

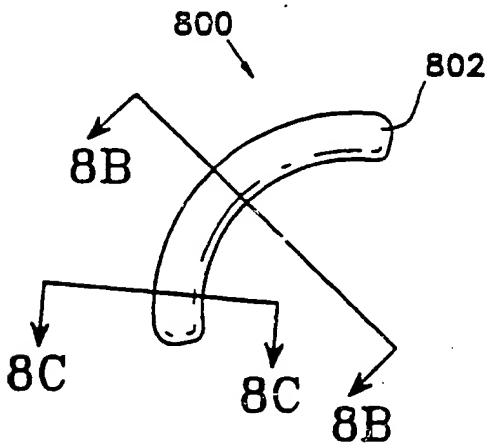


Fig. 8A

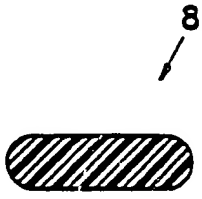


Fig. 8B

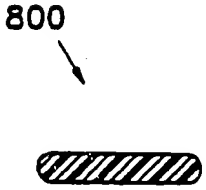


Fig. 8C

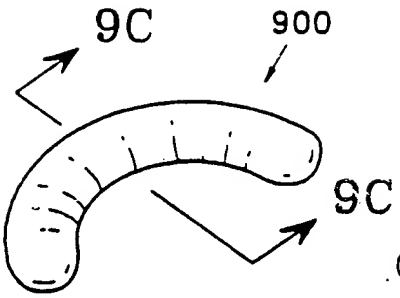


Fig. 9A

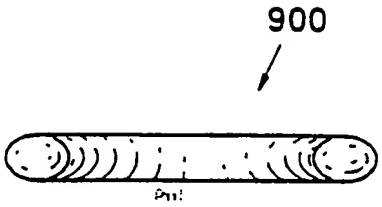


Fig. 9B

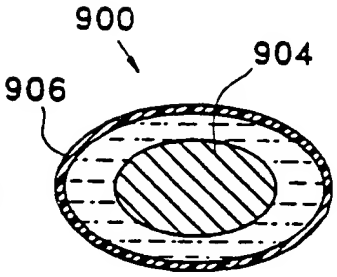


Fig. 9C

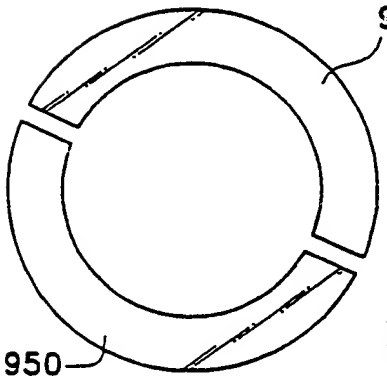


Fig. 10

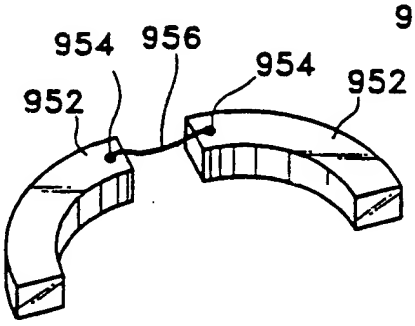


Fig. 11

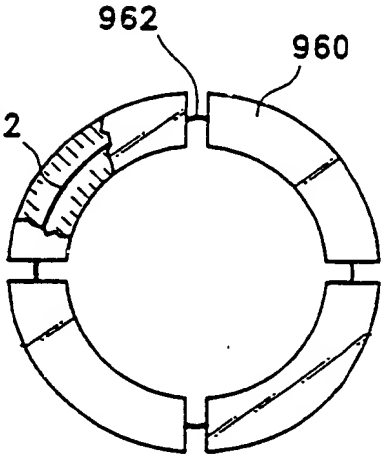


Fig. 12

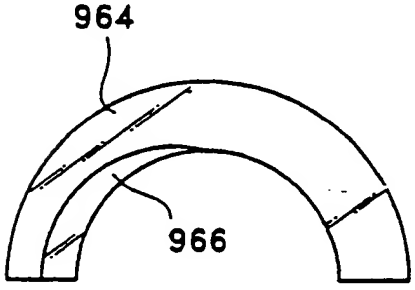


Fig. 13A

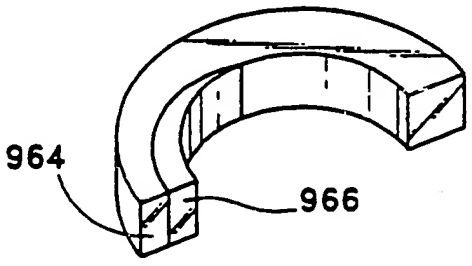


Fig. 13B

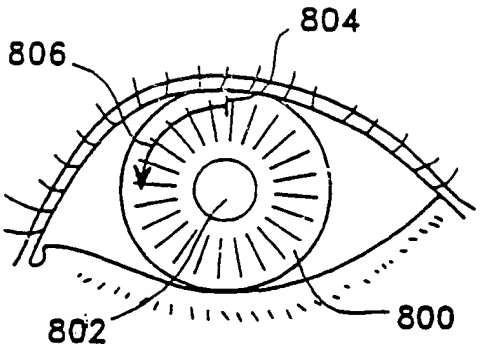


Fig. 14A

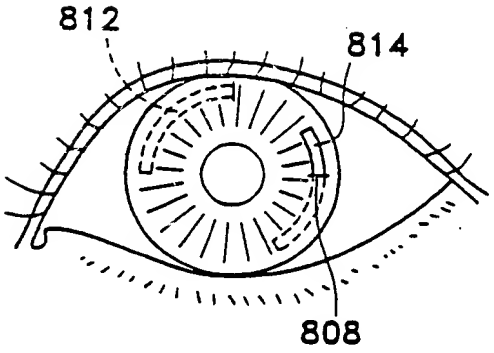


Fig. 14D

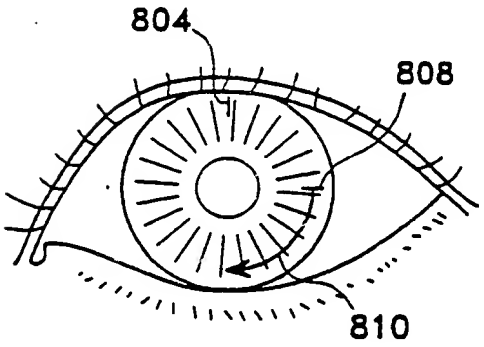


Fig. 14B

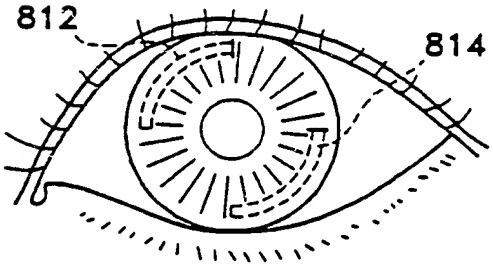


Fig. 14E

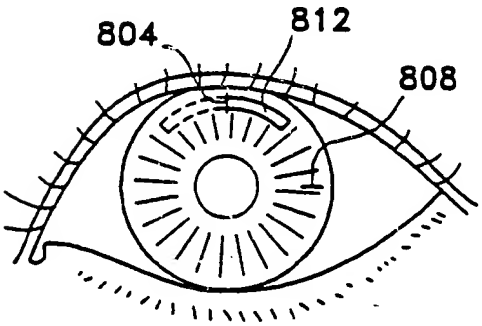


Fig. 14C

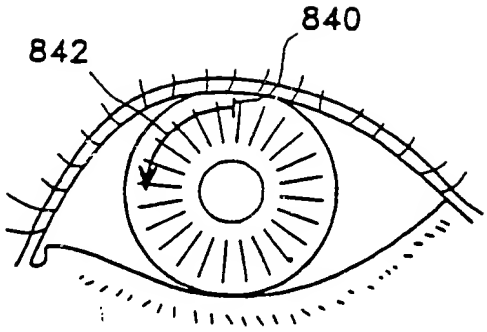


Fig. 15A

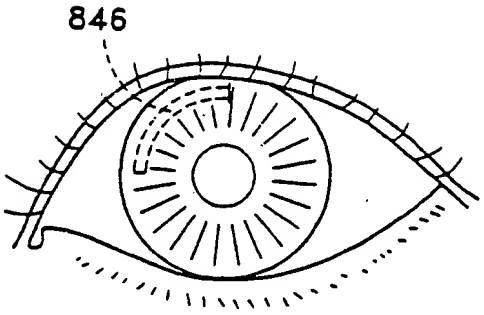


Fig. 15D

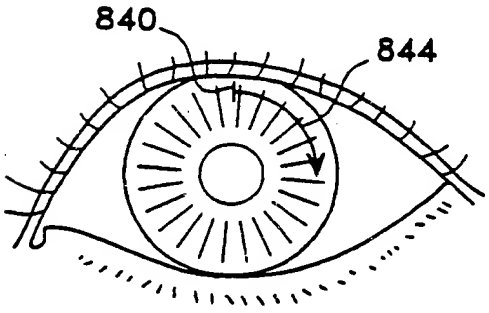


Fig. 15B

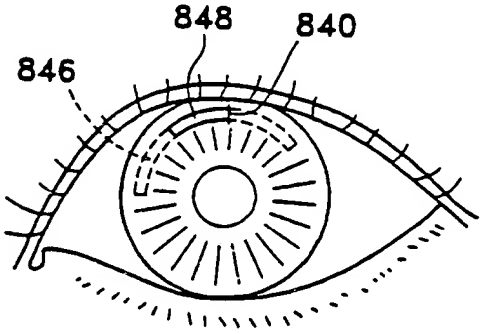


Fig. 15E

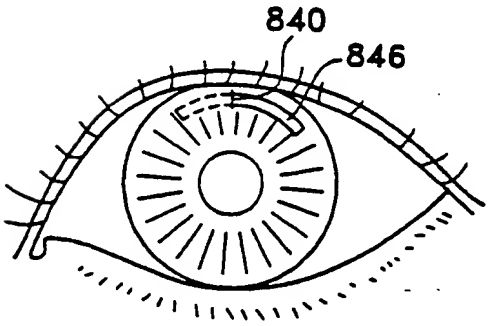


Fig. 15C

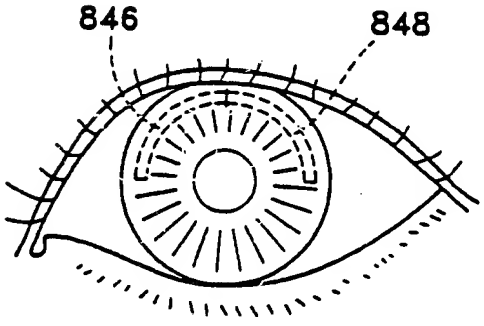


Fig. 15F

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/08462

A. CLASSIFICATION OF SUBJECT MATTER
IPC(5) :A61F 02/14
US CL :623/5
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/427, 428; 623/4, 5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US, A, 5,178,635, (GWON ET AL.), 12 January 1993. See entire document.	1-7, 14-25, 20-22
X	US, A, 4,290,426, (LUSCHEN ET AL.), 22, September 1981. See column 6 lines 62-66, column 7 lines 39-56, col.umn 9 lines 6-11, and Examples 3 and 4.	1-4, 7-22
X	US, A, 5,147,647, (DAROUGAR), 15 September 1992. See entire document.	1-15, 18-22
X	US, A, 4,014,335, (ARNOLD), 29 March 1977. See entire document.	1-7, 14-25

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be part of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 29 SEPTEMBER 1994	Date of mailing of the international search report 15 DEC 1994
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer RANDY C. SHAY Telephone No. (703) 308-2907

Form PCT/ISA/210 (second sheet)(July 1992)*